REMARKS/ARGUMENTS

Prior to the present amendments, Claims 49-63 were pending in this application. Claims 49, 52, and 53 were amended, Claims 54-63 were canceled. The amendments to Claim 49 are supported at least at page 6, lines 28-35, and page 12, lines 24-33. The rest of the claim amendments are of formal nature. The specification has been amended by adding a new corrected Sequence Listing and by supplementing the conditions of the ATCC deposit. Figure 5 has been replaced by a corrected Figure 5 containing all N-terminal nucleic acids. All amendments are fully supported by the specification as originally filed and do not add new matter.

Information Disclosure Statement

The Examiner notes that only the references initialed were found in the parent application, and that references Nos. 15-17 are not appropriate for an IDS since BLAST alignments should be appended as part of each individual reference, and each reference must be fully identified. The consideration of reference Nos. 15-17 is not necessary, since the individual references from within these BLAST results have been listed in the rest of the Information Disclosure Statement as Reference Nos. 21-199. Since the latter references, originally filed in the parent application, are apparently missing, Applicants hereby resubmit them with a Supplemental Information Disclosure Statement accompanying the present response. The Examiner is respectfully requested to acknowledge consideration of all references by returning an initialed copy of the current Supplemental Information Disclosure Statement.

Objections to the Specification

Claim 62 has been objected to for its recitation of "the host cell Claim 63." The cancellation of Claim 62 moots this objection.

Claim 52 was objected to for a typographical error, which has been corrected by the current claim amendments.

New Matter Issue

According to the Office Action, the preliminary amendment filed on August 22, 2005 introduced new matter, since SEQ ID NO: 11 contains nucleic acid 1306 as an "A," which is

different from the sequence set forth in Figure 5 filed with the application, where the nucleotide at position 1306 is "C." In addition, the Examiner notes that SEQ ID NO: 11 contains different N-terminal nucleotides from those present in Figure 5 filed with the application. Claims 49-63 were rejected under 35 U.S.C. §112, first paragraph, as allegedly containing "new matter" for the same reasons.

The error at position 1306 has been corrected so that SEQ ID NO: 11 lists a "C in that position.

The extra N-terminal nucleotides relative to Figure 5 filed with the present application have been retained for the following reasons. In Figure 5 filed with the present application, the first 11 N-terminal nucleotides were accidentally covered by the designation "SEQ ID NO: 11." However, correct Figure 5, including the entire sequence of SEQ ID NO:11, was included as Figure 2 in U.S. Provisional Patent Application Serial No. 60/066,364 filed on November 21, 1997, the entire disclosure of which was incorporated by reference into the present application at the time of filing. Accompanying the present response is a corrected Figure 5 and a copy of Figure 2 from U.S. Provisional Patent Application Serial No. 60/066,364. Also enclosed is a Declaration of Incorporation by Reference, stating that corrected Figure 5 shows the same sequence present in Figure 2 of U.S. Provisional Patent Application Serial No. 60/066,364, which is incorporated by reference in its entirety in the above-captioned application.

Accordingly, corrected Figure 5 and the Sequence Listing submitted with the present response do not constitute new matter, and their entry is respectfully requested. The Examiner is further requested to withdraw the related rejection of remaining Claims 49-53.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 53, 58, and 63 were rejected as "indefinite" in their recitation of "PRO301." Claims 58 and 63 have been canceled, and claim 53 has been amended by deleting the reference to PRO301, which is believed to obviate the present rejection.

Rejections Under 35 U.S.C. §112, First Paragraph

(1) Claims 49-63 have been rejected for alleged lack of enablement since the recitation of the conditions of the deposit of pRK5-based plasmid DNA40628-1216 was

incomplete. The deposit statement has been supplemented, as requested by the Examiner, therefore, the withdrawal of the present rejection of remaining Claims 49-53 is respectfully requested.

(2) Claims 49-53 and 59-63 were rejected under 35 U.S.C. §112, fist paragraph, for alleged lack of enablement. The Examiner has acknowledged that the specification is enabling for an isolated nucleic acid sequence of SEQ ID NO: 11 encoding SEQ ID NO: 1, an isolated nucleic acid sequence encoding a polypeptide of SEQ ID NO: 1, with or without the signal sequences, for inhibition of VEGF stimulated proliferation of endothelial cells, but holds that the claims reciting the deposit and the genus claims reciting "at least 95% sequence identity" or characterized by the ability to hybridize to SEQ ID NO: 11 are not enabled. According to the rejection, the rejected claims "encompass an unreasonable number of inoperative polynucleotides, which the skilled artisan would not know how to use." The Examiner adds that "function cannot be predicted based solely on structural similarity," and cites Altwood and Solnick in support of this point.

Without acquiescing in the rejection, or the Examiner's reasoning underlying the rejections and merely to advance prosecution, Claims 54-63 have been canceled, and Claim 49 is now directed essentially to subject matter for which the Examiner has acknowledged sufficient enablement. The claim extends to he full-length coding sequence of the cDNA deposited under ATCC accession number 209432, since the deposit was made under the conditions of the Budapest Treaty, which is now clearly reflected in the specification. In addition, the claim extends to a nucleic acid encoding the extracellular domain of the polypeptide of SEQ ID NO: 1. It is well established in the art that the extracellular domain (soluble version) of a protein can be the same way and for the same uses as the full-length protein itself.

The Examiner is respectfully requested to reconsider and withdraw this rejection with regard to the remaining claims.

(3) Claims 49-53 and 59-63 were rejected under 35 U.S.C. 112, first paragraph, as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) at the time the application was filed, has possession of the claimed invention. Citing Fiers v. Revel and the

Written Description guidelines, the Examiner notes that "the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics," and finds that the rejected claims do not meet this standard.

Without acquiescing in the rejection, or the Examiner's reasoning underlying the rejection, and solely to advance prosecution, Claims 54-63 have been canceled, and Claim 49 has been amended. The claims currently pending closely follow the specific disclosure provided in the specification, therefore, one of ordinary skill would clearly recognize that Applicants were in the possession of the invention as currently claimed. Accordingly, the withdrawal of the present rejection is respectfully requested.

Rejection Under 35 U.S.C. §102(e)

Claims 49-63 were rejected under 35 U.S.C. 102(e) as allegedly being anticipated by U.S. Patent No. 6,358,707, "as evidence by the specification on page 49, lines 36-39." According to the rejection, the '707 patent teaches and claims the full-length coding sequence of nucleic acid having 100% sequence identity to the claimed SEQ ID NO: 11 encoding a polypeptide that has 100% sequence identity to SEQ ID NO: 1 of the present application.

The rejection is respectfully traversed.

The U.S. application on which the '707 patent issued is a national stage application under 35 U.S.C. §371 filed on January 5, 2000. Since this precedes November 29, 2000 and the U.S. application was not voluntarily published, the 102(e) date of the '707 patent is January 5, 2000. This is clearly reflected on the front page of the patent. Since the present application, as the Examiner has acknowledged, is entitled to at least the November 20, 1998 priority date, the '707 patent is not prior art under 35 U.S.C. 102(e). Accordingly, the present rejection is believed to be misplaced, and should e withdrawn.

Applicants note that the PCT application corresponding to the '707 patent was first published on January 21, 1999 (WO 99/02561), and is therefore not prior art either.

Rejection Under 35 U.S.C. §103(a)

Claims 49-63 were rejected under 35 USC 103(a) as allegedly obvious over Naik *et al.* (1995), as is evidenced by Sobocka *et al.*, in view of Alberts *et al.* (1989).

Naik *et al.* was cited for its teaching of the F11 antigen. According to the rejection Naik *et al.* also teach that "the N-terminal 26 amino acid sequences of the F11 antigen, which has 32 and 35 kDa protein, were identical and contained a single unblocked serine in the N-terminal position." The Examiner adds that "when digested with N-glycanase, the 32 and 35 kDa proteins were converted into a single ~29 kDa protein, indicating that these two proteins are derived from the same core protein but differ in their degree of glycosylation." The Examiner acknowledges that Naik et al. do not disclose SEQ ID NO: 1, but cites post-published Sobocka et al. that Naik *et al.* in fact had a polypeptide identical to the polypeptide of SEQ ID NO: 1 of the present invention. Alberts was cited as allegedly teaching that once a protein is purified to homogeneity, its biological activities can be examined in detail, and that it is now easy to produce a "genomic DNA clone," by excising any region of a cell's DNA and inserting into a plasmid. The Examiner concludes that it would have been obvious to one skilled in the art at the time the invention was made "to determine the rest of the F11R amino acid sequence taught by Naik *et al.* using the genetic engineering techniques and its gene can be cloned, express the DNA using the vectors, host cells and the method of producing the polypeptide as taught by Albert *et al.*

The rejection is believed to be misplaced, and is vigorously traversed.

Naik *et al.* (1995) partially purified the F11 protein and determined a 26 amino acids long sequence, designated as the "N-terminal sequence," along with some additional short internal sequences. Sobocka *et al.* (2000), which was published after the priority date of the present application, is cited as evidence that the partially purified polypeptide of Naik *et al.* is a polypeptide (F11), which is identical to PRO302 of SEQ ID NO: 1 of the present application. What the Examiner fails to point out is that Sobocka et al. also show that Naik *et al.* incorrectly assigned the N-terminus of their polypeptide. In fact, the 26-amino acid sequence of Naik *et al.* is an internal sequence of F11, and not the correct N-terminal sequence.

Furthermore, the Examiner's attention is respectfully directed to In re Bell, 991 F.2d 781, 26 USPQ2d 1529 (Fed. Cir. 1993), holding that the established relationship between a nucleic acid and the protein it encodes does not render a gene *prima facie* obvious over its corresponding

protein in the same way that closely related structures in chemistry may create a *prima facie* case because there are a vast number of nucleotide sequences that might encode for a specific protein as a result of degeneracy in the genetic code. Similarly, In re Deuel, 51 F.3d 1552 (Fed. Cir. 1995) held that a "prior art disclosure of the amino acid sequence of a protein does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein." The existence of a general method of gene cloning in the prior art is not sufficient, without more, to render obvious a particular cDNA molecule. Fully consistent with these decisions, in Amgen v. Chugai the Federal Circuit confirmed that conception of a DNA invention "has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated." 927 F.2d 1200 (Fed. Cir.), *cert. denied*, 502 U.S. 856 (1991), at 1206.

In view of the well establish case law, the prior disclosure of a partially purified protein and some short internal stretches of amino acid sequences within that protein does not render obvious the nucleic acid molecules claimed in the present application. Therefore, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

All claims pending in this application are believed to be in *prima facie* condition for allowance, and an early issuance of a Notice of Allowance is respectfully solicited.

Although no fees are believed to be due at this time, please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney Docket No. **39780-1216 R1D4**).

Respectfully submitted,

Date: December 20, 2005

By: _____
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